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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KAPUST, RACHEL B	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,011	DAMBINOVA, SVETLANA A.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-45 and 63-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-45 and 63-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

Applicant's amendment filed April 9, 2004 is acknowledged. Claims 1-40 and 46-62 have been canceled. Claims 41-45 have been amended. Claims 63-65 are new. Claims 41-45 and 63-66 are pending and under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification regarding the use of trademarks is withdrawn in response to Applicant's amendments to the specification.

The objection to claim 45 regarding a typographical error is withdrawn in response to Applicant's amendment changing the word "autobody" to "autoantibody".

The rejection of claims 41-45 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn in response to Applicant's amendments to the claims. The claims are now drawn to the diagnosis of a "neurological ischemic deficit" which is the shortage of blood flow to part of the brain.

The rejection of claims 41-43 and 45 under 35 U.S.C. 102(b) as being unpatentable over Dambinova *et al.* is withdrawn in response to Applicant's amendments to the claims. Dambinova *et al.* do not teach measuring levels of NR2A and/or NR2B NMDA receptors and agonists or antagonists thereof by latex agglutination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 41-43, 45, and 63-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dambinova *et al.* and in view of Senju *et al.* (1986, *J. Clin. Lab. Immunol.* 19(2): 99-103). Applicant argues that Dambinova *et al.* do not anticipate the claimed invention because the pending claims as amended require the diagnosis to be via latex agglutination, and Dambinova *et al.* disclose testing via undisclosed alternative methods (see response, p. 7). Applicant also argues that Dambinova *et al.* do not anticipate the pending claims because the pending claims require that a "diagnosis" occur (see response, p. 7).

As stated in the previous office action, Dambinova *et al.* teach a direct method of detection of NR2A NMDA receptors by immunopurification and an indirect method of detection by detecting autoantibodies to NR2A NMDA receptors in stroke patients. Dambinova *et al.* also teach measuring glutamate and aspartate concentrations in stroke patients. Although Applicant argues that Dambinova *et al.* do not require that a diagnosis occur, Dambinova *et al.* state that the "present study is an attempt to show that autoantibodies to subtypes of glutamate receptors can be a means for determination of persons having brain paroxysmal activity or brain ischemic stroke" (p. 151, column 2). Dambinova *et al.* stress the importance of having an objective laboratory instrument to provide for the accurate and early diagnosis of central nervous system diseases, and Dambinova *et al.* clearly anticipate using the method in the diagnosis of CNS diseases as they state that "the raised level of autoantibodies to both of fragments of glutamate receptors could be an indicator of the development of cerebrovascular functional abnormalities" (p. 154, column 1). Claims 63-65 are drawn to methods of diagnosing neurological ischemic deficits, wherein the neurological ischemic deficit is either predictive of a past incident of stroke or TIA or predictive of a future incidence of stroke or TIA. Claim 66 is drawn to a method of

diagnosing neurological ischemic deficits wherein the results of the diagnosis are communicated to the patient. Dambinova *et al.* teach that "detection of autoantibodies to immunologically active peptide fragments of glutamate-binding proteins could successfully be used not only for diagnosis of disorders but also for daily clinical monitoring of patients" (p. 154, column 2). This would encompass both prediction of past incidences of stroke and TIA and also future incidences of stroke or TIA. Communicating any results to the patient would be an inherent part of the method. However, the claims as amended are now drawn to measuring the level of NR2A and/or NR2B NMDA receptor and agonists thereof by latex agglutination, and Dambinova *et al.* do not teach this limitation.

Senju *et al.* teach using latex agglutination as an immunoquantitative method. Senju *et al.* teach that latex agglutination is more rapid and sensitive than enzyme immunoassay and radioimmunoassay (p. 99). It would have been obvious to a person of ordinary skill in the art to modify the method as taught by Dambinova *et al.* by measuring the NR2A NMDA receptor and its agonists via latex agglutination rather than ELISA. Motivation to do so is provided by Senju *et al.* who teach that latex agglutination is more rapid and sensitive than enzyme immunoassays. One of ordinary skill in the art would have expected the modified method to be as successful in diagnosing a neurological ischemic deficit as that taught by Dambinova *et al.*

Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dambinova *et al.* (1997) and Senju *et al.*, as discussed above, in view of Daggett *et al.* (U.S. Patents 6,316,611 and 5,849,895). Specifically, Dambinova *et al.* teach measuring the level of NR2A NMDA receptors in stroke patients by measuring the levels of autoantibodies to the receptors, an indirect method, and by measuring the amount of NR2A NMDA receptor directly by immunopurification, a direct method. However, Dambinova *et al.* do not teach a method of indirectly measuring the level of NR2A NMDA receptor in stroke patients by measuring the amount of NR2A NMDA receptor mRNA. In the 5,849,895 patent, Daggett *et al.* teach an indirect method of detection of NR2A NMDA receptor by detecting NR2A NMDA receptor mRNA (column 9, line 63 through column 10, line 12). Daggett *et al.* also teach an indirect method of RNA detection by identifying NR2A NMDA receptor cDNA (column 8, lines 26-39 in the 5,849,895 patent). It would have been obvious to a person of ordinary skill in the art to combine the methods as taught by Daggett *et al.*

with the method as taught by Dambinova *et al.* and Senju *et al.* One of ordinary skill in the art would have been motivated to do so because Dambinova *et al.* teach that detecting NR2A NMDA receptors are useful for diagnosing strokes, and the 5,849,895 and 6,316,611 patents teach alternative means of detecting NR2A NMDA receptors that one of ordinary skill in the art would have expected to be equally useful. Therefore, the invention taken as a whole is *prima facie* obvious over the prior art.

Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dambinova *et al.* and Senju *et al.* in view of Lipton *et al.* As previously stated, Dambinova *et al.* teach both indirect and direct methods of measuring the level of NR2A NMDA receptor in stroke patients. Moreover, Dambinova *et al.* teach that measuring NR2A NMDA receptor levels is useful for diagnosing strokes. However, Dambinova *et al.* do not teach measuring homocysteine levels in stroke patients. Lipton *et al.* teach that there is an association between homocysteine and cerebrovascular disease and that it can directly cause neurotoxicity by activating NMDA receptors (p. 5923). Lipton *et al.* further teach that elevated levels of homocysteine in the blood are diagnostic of arteriosclerosis and stroke. Because each method is useful for the same purpose, it would be *prima facie* obvious to combine the two methods in order to form a combination that is to be used for the very same purpose. See *In re Kerkhoven* (205 USPQ 1069, CCPA 1980). One of ordinary skill in the art would have been motivated to combine the methods of Dambinova *et al.* and Senju *et al.* and Lipton *et al.* because they are both useful for diagnosing strokes.

Conclusion

NO CLAIMS ARE ALLOWED.

The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon are considered pertinent to the instant application:

Pang *et al.* (1988), *Jpn. Heart J.* 29(5): 631-638

Gray *et al.* (1987), *J. Virol. Meth.* 16: 13-19

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBK
6/21/04

JANET ANDRES
PATENT EXAMINER